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Antimony and Sleep-Related Disorders: NHANES 2005–2008

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Abstract

Background—Antimony is used as a flame-retardant in textiles and plastics, in semiconductors, pewter, and as pigments in paints, lacquers, glass and pottery. Subacute or chronic antimony poisoning has been reported to cause sleeplessness. The prevalence of short sleep duration (<7 hours/night) has been reported to be 37.1% in the general US population, and obstructive sleep apnea (OSA) affects 12–28 million US adults. Insufficient sleep and OSA have been linked to the development of several chronic conditions including diabetes, cardiovascular disease, obesity and depression, conditions that pose serious public health threats.

Objective—To investigate whether there is an association between antimony exposure and sleep-related disorders in the US adult population using the National Health and Nutrition Examination Survey (NHANES) 2005–2008.

Methods—We performed multivariate logistic regression to analyze the association of urinary antimony with several sleep disorders, including insufficient sleep and OSA, in adult (ages 20 years and older) participants of NHANES 2005–2008 (n=2654).

Result—We found that participants with higher urinary antimony levels had higher odds to experience insufficient sleep (≤ 6 hours/night) (OR 1.73; 95%CI; 1.04, 2.91) as well as higher odds to have increased sleep onset latency (>30 minutes/night). Furthermore, we found that higher urinary antimony levels in participants were associated with OSA (OR 1.57; 95%CI; 1.05, 2.34), sleep problems, and day-time sleepiness.

Conclusion—In this study, we found that urinary antimony was associated with higher odds to have insufficient sleep and OSA. Because of the public health implications of sleep disorders, further studies, especially a prospective cohort study, are warranted to evaluate the association between antimony exposure and sleep-related disorders.

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INTRODUCTION

Antimony is a silvery white metal that is commonly found within the Earth's crust (ATSDR 1992). Antimony exists in either a trivalent or pentavalent state. Because antimony occurs naturally within the Earth's crust, it is released into the environment through natural processes, including dust, volcanic ash, and forest fire residue. Additionally, exposure to and toxicity from antimony may arise due to occupational exposure, domestic use, or when it is used as a medical therapy (McCallum 2005; Sundar and Chakravarty 2010). Antimony is used to treat parasitic diseases including leishmaniasis and schistosomiasis. Furthermore, antimony is used in semiconductors and pewter, as a fire-retardant in textiles and plastics, and as a pigment in paints, lacquers, glass and pottery (McCallum 2005).

The general US population is exposed to measurable levels of antimony in the environment, primarily through food and, to a lesser extent, from air and drinking water (Navas-Acien et al. 2005). Dermal contact with soil, water, or other substances containing antimony is another means of exposure. The absorption, distribution, and excretion of antimony vary depending on its oxidation state, with urinary excretion appearing to be greater for pentavalent antimony compounds than for trivalent compounds (Elinder and Friberg 1986). An elimination half-life of approximately 95 hours has been estimated after occupational exposures for the trivalent form (Kentner et al. 1995) and 24 hours for the pentavalent form (Gebel 1997). Furthermore, human health effects from antimony at low environmental doses or at biomonitored levels from low environmental exposures are not well known.

Studies have shown that most of the antimony that enters the body concentrates in the liver, lungs, intestines, and spleen (ATSDR 1992). Exposure to antimony can cause irritation of the nose, throat, skin, and mouth, as well as nausea and loss of sleep (NJDOH 2004). Chronic inhalation of low levels of antimony can result in lung problems (e.g., pneumoconiosis), heart problems (including increased blood pressure and altered electrocardiograms), and stomach pain, diarrhea, vomiting and stomach ulcers (ATSDR 1992; Cooper and Harrison 2009, Sundar and Chkravarty 2010).

The most comprehensive information on health effects following acute and subacute antimony poisoning comes from a self-administered experiment conducted by Mayerhofer (1846). Following ingestion of small doses of tartarized antimony at increasing frequencies, Mayerhofer reported sleep disturbance (1846). Sleeplessness after subacute and chronic antimony poisoning has also been reported (Stemmer 1976; WHO 2003); however, there is a deficiency in research surrounding this potential association. Insufficient sleep has been a risk factor to the development of several chronic conditions including diabetes, cardiovascular disease, obesity and depression; these conditions have, in turn, been linked to sleep disorders. and cardiovascular diseases have been associated with antimony exposure (Guo et al. 2016; Nigra et al. 2016) Additionally, genetic factors and other behavioral characteristics, such as alcohol use, smoking, obesity, marital status, and income, can contribute to the development of sleep-related disorders. The National Heart, Lung, and Blood Institute (NHLBI) recommends that adults get 7–8 hours of sleep per day (NHLBI 2011). The prevalence of short sleep duration (<7 hours on weekday or workday nights) has been reported to be 37.1% in the general US population (CDC 2011). Sleep insufficiency

and poor sleep quality can also result from sleep disorders such as chronic insomnia, obstructive sleep apnea (OSA), restless legs syndrome, or narcolepsy (IOM 2006).

Because of the ubiquitous exposure to antimony in the general population, the public health consequences of sleep disorders, and the potential but largely unexplored relationship between the two, the objective of this study was to investigate the potential association between antimony exposure with sleep duration, sleep onset latency time, and sleep-related disorders in the adult population using the National Health and Nutrition Examination Survey (NHANES) 2005–2008. We hypothesize that population level exposures to antimony are associated with sleep related disorders.

METHODS

Study population

NHANES is a cross-sectional, nationally representative survey of the non-institutionalized civilian population of the United States conducted by the National Center for Health Statistics (NCHS), CDC (NCHS 2008a). Beginning in 1999, the survey has been conducted continuously and released in 2-year cycles. The NHANES 2005–2006 and 2007–2008 are the only cycles where a complete questionnaire about sleep habit and disorders were performed, so that several outcomes could be defined. For our study we merged the publicly available files for NHANES cycles 2005–2006 and 2007–2008 using the NCHS recommendations (NCHS 2008b). The survey employs a multistage stratified probability sample based on selected counties, blocks, households, and persons within households.

NCHS-trained professionals conducted interviews in participants' homes. Extensive physical examinations, including blood and urinary collection, were conducted at mobile exam centers (MECs). CDC's National Center for Environmental Health (NCEH), Division of Laboratory Sciences (DLS), coordinates the National Biomonitoring Program (NBP) which offers an assessment of nutritional status and the exposure of the US population to environmental chemicals and toxic substances. In the 2005–2006 and 2007–2008 data sets, urinary concentrations of antimony were measured in a randomly selected one-third subsample.

All procedures were approved by the NCHS Research Ethics Review Board (Continuation of Protocol #2005–2006 http://www.cdc.gov/nchs/nhanes/irba98.htm), and all participants provided written informed consent. The unweighted response rate for adult participants 20 years of age and older for NHANES 2005–2006 and NHANES 2007–2008 were 70.4% and 70.6%, respectively (NCHS 2006; NCHS 2008c) (Of the participants who answered questions for the sleep questionnaire, we included only those participants who had measurements for urinary antimony (n=3,328). Pregnant (n= 102) and breastfeeding (n=27) women were excluded from our analyses. Additionally, participants with missing information on *a priori* covariates adjusted for in the multivariate analyses, for example education (n=1), body mass index (n=55), income (n=221), serum cotinine (174), were excluded from our analysis for a final, total sample size of 2.654 participants.

Outcome

We investigated the following self-reported prevalent outcomes that are related to sleep disorders: sleep duration, sleep-onset latency, OSA, sleep problems, and day-time sleepiness. These outcomes were defined in the following ways:

- Sleep duration: categorized as insufficient (≤ 6 hours/night), normal (7–8 hours/night), or excessive (≥ 9 hours/night) (National Sleep Foundation 2009, Plantinga et al. 2012).
- Sleep-onset latency: categorized as normal (6–30 minutes/night), prolonged (> 30 minutes/night), or short (≤ 5 minutes/night) which may be indicative of having a sleep disorder (Dement and Vaughn 2009, Plantinga et al. 2012).
- Obstructive sleep apnea (OSA): characterized according to Healthy People 2020 (Healthy People 2020) and was defined as any of the following: doctor diagnosed sleep apnea; or snoring 3 or more nights per week; or snorting, gasping or stopping breathing 3 or more nights per week; or (feeling excessively sleepy during the day 16–30 times per month despite sleeping around 7 or more hours per night on weekdays or work nights).
- Sleep problems: considered frequent if self-reported “often” or more (≥ 5 times/month) (Plantinga et al.2012) in response to any of the following questions from the NHANES sleep questionnaire: “Have you ever told a doctor or other health professional that you have trouble sleeping?”; “In the past month, how often did you have trouble falling asleep?”; “In the past month, how often did you wake up during the night and had trouble getting back to sleep?”; or, “In the past month, how often did you wake up too early in the morning and were unable to get back to sleep?”. (Plantinga et al.2012)
- Day sleepiness: considered frequent if self-reported “often” or more (≥ 5 times/month) (Plantinga et al.2012) in response to any of the following questions from the NHANES sleep questionnaire: “In the past month, how often did you feel unrested during the day, no matter how many hours of sleep you have had?” or “In the past month, how often did you feel excessively or overly sleepy during the day?”.

Urinary Biomarkers

Spot urine samples were collected from study participants and stored at −20°C; they were then analyzed by NCEH/DLS. Urinary antimony was measured by inductively coupled plasma-mass spectrometry using a multi-element analytical technique. The interassay coefficient of variation range from 3.1% to 5.6%. Details of detection and measurement of the urinary compounds are described in the NHANES laboratory method (NCHS 2007)

Urinary antimony was categorized by a weighted quartile distribution based on the distribution of urinary antimony levels among the study population, resulting in approximately the same number of participants within each quartile. Due to their association with antimony exposures (McCallum 2005), urinary lead and urinary arsenic were entered into the models as natural log- transformed variables. The limits of detection (LODs) for

urinary antimony was 0.03 μg/L. Urinary concentrations of antimony below the LOD were assigned the LOD divided by the square root of 2, as recommended by NHANES (NCHS 2007). There were 22.6% participants with urinary antimonybelow the limit of detection. To account for variation in dilution in spot urinary samples, urinary creatinine was entered in the analyses as an independent variable as suggested by previous studies (Barr et al. 2005; Ikeda et al. 2003). Urinary creatinine was determined using a Jaffé rate reaction measured with a CX3 analyzer, and it was entered into the model as a natural log-transformed variable.

Covariates

The regressions models were adjusted for covariates that have been associated with sleep disorders: age (categorized in weighted quartile), sex, race/ethnicity, education level (Eshkoor et al. 2013; Grandner et al. 2013; Kim et al. 2013), income level (Eshkoor et al. 2013; Grandner et al. 2013; Kim et al. 2013), alcohol consumption (Strine and Chapman 2005), smoking status (Cohrs et al. 2014; Kim et al. 2012), body mass index (Hasler et al. 2004; Taheri et al. 2004), and shift work (IOM 2006). Serum cotinine, a biomarker of exposure to environmental tobacco smoke was also entered into the models.

We obtained information about age (years), sex, race/ethnicity, education level, and income level from the household interview. Race/ethnicity were categorized as non-Hispanic white, non-Hispanic black, Hispanic (Mexican-American and Other Hispanic), and other. Education was divided into those who had completed less than high school, completed high school, and completed some school more than high school. Income is based on poverty income ratio that represents the calculated ratio of household income to the poverty threshold after accounting for inflation and family size, with income values <1 representing those below the poverty line; this was entered as a continuous variable in the models. Alcohol consumption (amount consumed per week) and smoking information were obtained from the associated questionnaires. Alcohol was categorized as no alcohol use, 1–4 drinks per week, and >4 drinks per week. Cigarette smoking was defined as never-smoker (smoke < 100 cigarettes ever), former smoker (not currently smoking, but has smoked ≥100 cigarettes ever), and current smoker. Body Mass Index (BMI) is calculated by the weight divided by height squared (kg/m^2).

In the final model we entered diabetes, cardiovascular diseases, physical and mental health, as these chronic conditions have been associated with sleep disorders, and occupation. Cardiovascular diseases (CVD) was defined as having hypertension or having a positive response to any of the following statements: “ever told you had congestive heart failure,” “ever told you had coronary heart disease,” “ever told you had angina/angina pectoris,” “ever told you had a heart attack,” or “ever told you had a stroke.” Physical and mental health status were obtained from the current health status questionnaire where the participants were asked “During the past 30 days, for about how many days did poor physical or mental health, which includes stress, depression, and problems with emotions, keep you from doing usual activities, such as self-care, work, school or recreation?” The Variable for occupational work was obtained from the occupational questionnaire. The occupational data were categorized, on the basis of the participant’s current job, which was defined as the main paid job worked within the last week, as follows: 1) looking for work or

not working at a job or business; 2) currently working at job with a regular daytime working schedule, and; 3) currently working at a job with a regular night/evening working shift/ rotating shift/other schedule.

Statistical Methods

SAS 9.3 (SAS Institute, Cary, NC) was used for all statistical analyses and SAS-Callable SUDAAN 10 (Research Triangle Institute, Research Triangle Park, NC) was used to account for the NHANES complex sample design. P-values were presented at the significance level of 0.05. All analyses were performed using the sample weights specific for the one-third subset of participants with urinary antimony measurements to account for the complex sampling design and non-response bias of NHANES. Weights for combined NHANES survey cycles were calculated according to NHANES guidelines (NCHS 2008b). Statistical tests for linear trends were conducted by modeling quartiles as an ordinal variable using integer values.

We used the MULTILOG procedure in SUDAAN, which implements the proportional odds model with a generalized multinomial logit model for nominal outcomes. This calculation produces separate parameter vectors for each of the generalized logit equations of interest to calculate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) (significant at p-value<0.05) for the outcomes of sleep onset latency and sleep time duration. We used logistic regression to calculate adjusted ORs and 95% CIs for the other sleep disorder outcomes. Three models were evaluated for each sleep-related outcome: model 1 was adjusted for urinary creatinine; model 2 was further adjusted for demographic and socio behavioral variables, such as sex, age, race/ethnicity, education, alcohol consumption, self-reported smoking status, serum cotinine (natural log-transformed), and BMI; model 3 was adjusted for the covariates in model 2 plus diabetes, CVD, physical/mental health; and occupation. As complementary analyses we evaluated also the association between natural log-transformed urinary antimony and sleep-related outcomes.

RESULTS

The sample size of the study was 2,824, representing a population size of 182,928,057.50 US adults (20 years and older). The characteristics of the study population are presented in Table 1. The geometric mean (GM) age of the participants was approximately 44 years. Among the participants, 72.78 % were Non-Hispanic whites and 51.14% were females. Approximately 57%, 29%, and 51% of the people reported that they had attended some college, never used alcohol, and never smoked, respectively. The geometric mean (standard error of the geometric mean) urinary antimony level is0.06 (0.00) μg/L. Almost 37% of participants reported getting less than 7 hours of sleep per night, whereas only 7.16% of participants reported getting 9 hours of sleep or more per night. Thirty percent of participants reported falling asleep in 5 minutes or less, which may indicate extreme sleep deprivation (Dement and Vaughn 2009). In contrast, 18.20% of participants reported taking more than 30 minutes to fall asleep. Thirty-two percent of participants reported having sleep problems, a combination of having trouble falling asleep, waking up during the night, or waking up too early in the morning; almost 19% of participants reported feeling overly

sleepy during the day. OSA was reported in 36.34% of participants (Table 1). Supplemental Table 1 present the weighted characteristics of the population by urinary antimony quartile.

Sleep Duration and Onset Latency

In multivariable logistic regression analyses (adjusted for urinary creatinine), there were statistically significant associations of urinary antimony levels with insufficient sleep (≤ 6 hours/night) as opposed to adequate sleep (7–8 hours/night) (Table 2, Model 1). Further adjustment (Table 2, Model 2 and Model 3) did not change the associations: participants in the second, third, and fourth quartiles of urinary antimony had higher odds to experience insufficient sleep [OR (95% CI): 1.66 (1.19, 2.31); 1.93 (1.33, 2.79); and 1.73 (1.04, 2.91), respectively] compared to those in the referent quartile (Table 2, Model 3). Complementary analyses using natural log-transformed urinary antimony showed that there was a linear association between insufficient sleep duration and antimony [OR (95% CI): 1.22 (1.01, 1.46)] (Table 1).

Analyses of sleep-onset latency found that participants in the third and fourth quartiles of urinary antimony had higher odds to experience prolonged sleep-onset latency (more than 30 minutes per night) to fall asleep [OR (95% CI): 1.47 (1.04, 2.09) and 1.41 (1.01, 1.99), respectively] compared to participants in the lowest, referent quartile (Table 3, Model 3). Complementary analyses using natural log-transformed urinary antimony showed that association between prolonged sleep-onset latency and urinary antimony was linear model 1, but when all the covariates were entered in the models 2 and 3 the association was not anymore statistically significant, indicating that the association was not linear (Table 3).

Obstructive Sleep Apnea and Other Sleep-Related Problems

There was higher odds to have OSA in participants for all quartiles of exposure above the reference antimony level (>0.03 μg/L) (p-trend < 0.01), with significant associations for the second and fourth quartiles of urinary antimony [OR (95% CI): 2.09 (1.50, 2.92) and 1.57 (1.05, 2.34), respectively] (Table 4, Model 3). However, in complementary analyses there was no statistically significant association between OSA and natural log-transformed urinary antimony indicating that the association was not linear (Table 4)

Similarly, participants in all quartiles of exposure above the reference level had higher odds to experience sleep problems (p-trend = 0.08), with significant associations for the fourth quartiles of urinary antimony [OR (95% CI): 1.55 (1.08, 2.23) (Table 4, Model 3). Sensitivity analyses however, showed no linear statistically significant association when antimony was natural log-transformed (Table 4).

There was a U shape association between daytime sleepiness and urinary antimony. Participants in all quartiles of exposure above the reference level had higher odds to experience daytime sleepiness (p-trend = 0.02), with significant associations for the second and fourth quartiles of urinary antimony [OR (95% CI): 1.51 (1.00, 2.26) and 1.73 (1.03, 2.90), respectively] (Table 4, Model 3). Sensitivity analyses showed a linear statistically significant association when antimony was natural log-transformed (Table 4).

DISCUSSION

To our knowledge, this is the first reported association between urinary antimony levels with insufficient sleep and OSA in the US general population. We found that participants with higher urinary antimony levels had higher odds to experience insufficient sleep duration (≤ 6 hours/night) as well as higher odds to have prolonged sleep onset latency (>30 minutes/night). Furthermore, we found that OSA, sleep problems, and day-time sleepiness were associated with higher urinary antimony levels in participants.

The most detailed study on the human health effects of acute/subacute exposure to antimony comes from the pioneering work of Mayerhofer (1846), who self-administered repeated small doses of tartarized antimony. Mayerhofer dissolved a grain (64.80 mg) of tartar emetic (corresponding to 23.32 mg of antimony salt) in 100 drops of distilled water and took it over a period of 15 days at incremental doses. For the first 5 days he took one drop daily, with no adverse effects. On the 6^{th} day, he increased the dosage to a drop three times a day after which he reported disturbed sleep. With increase dosage in the following 9 days, the very restless sleep continue and new signs and symptoms were described such as anxiety constriction of the throat with trouble breathing, loss of power in the limbs, fever and head congestion, great oppression in the heart region, small and uneven pulse, and an increase in viscous mucus secretion from the bronchi and the trachea (Mayerhofer 1846).

Association between subacute or chronic antimony poisoning and sleepiness was also reported by Stemmer (1976). Additionally, there have been recently reported cases of cerebellar ataxia induced by pentavalent antimonial drug (Khalil et al. 2006), and sleep disorders are a common occurrence in neurodegenerative disorders such as cerebellar ataxia (Pedroso et al. 2011; Velázquez-Pérez et al. 2011). Edema of the upper airway is involved in the pathogenesis of OSA (Dempsey et al. 2010), and acute airway obstruction due to edema of the larynx with progressive difficulty in breathing has been reported after antimony therapy in mucosal leishmaniasis (Costa et al. 1986).

There are few studies that investigate chemical exposures with sleep-related disorders. These studies have found that occupational exposure to organic solvents is associated with obstructive sleep apnea and other sleep related problems (Reviewed in Viaene et al. 2009). Additionally, Kawada and colleagues (2005) reported that victims of sarin exposure in the Tokyo subway train event in 2003 experienced significantly higher prevalence of sleep related disorders including poor sleep and early morning awakening. Our study will add to this body of evidence suggesting that chemical exposure may affect sleep-related disorders by providing the first population-based study with antimony measurements.

Sleep disorders and sleep loss are among the most common health problems; however, despite their easy treatment, they are often overlooked. There are many far-reaching public health consequences of sleep loss and sleep-related disorders, including mortality, morbidity, accidents and injuries, family well-being, functioning and quality of life, and health care utilization. Sleep loss and OSA can affect the cardiovascular, endocrine, immune, and nervous systems; some of these wide-ranging effects include obesity in adults and children,

diabetes, cardiovascular disease and hypertension, anxiety symptoms, alcohol use, and depressed mood.

The US Geological Survey reported that industrial consumption of primary antimony in the US increased by 7% from 8050 metric tons of antimony content in 2012 to 8620 metric tons in 2013. One-third of primary antimony use is in flame-retardants, with the remaining antimony used in ceramics, glass, and lead-base alloys. Secondary antimony, which was derived almost entirely from recycled lead-acid batteries and present in antimonial lead, was used in the manufacturing of new batteries (USGS 2013). Notwithstanding the large industrial use of antimony, there is a paucity of information pertaining to the effects of antimony exposure in the general population.

This study used the NHANES 2005–2008 dataset, a large, national survey whose findings are generalizable to the US adult non-institutionalized population. Although there are strengths to this study, including its large sample-size and random sampling, there are important limitations to note. For example, this study uses a cross-sectional study design, which limits the inferences that can be made based on the findings because temporality between exposure and outcome cannot be established. Furthermore, the self-reported information on sleep loss, sleep apnea, and other sleep problems without further objective measures or clinical assessment may have led to reporting bias. The association reported in this study could be biased by uncontrolled confounders such as genetic predisposition or some other unknown factor that could be linked to both antimony levels and sleep disturbance. However, the models were adjusted for several likely important confounding factors (sex, age, race/ethnicity, education status, annual income, obesity, alcohol, smoking status, several chronic diseases related to sleep-disorders, and occupational information). The half-life of antimony depends on the isotope, with most being eliminated from the body in four days (the trivalent form) or 24 hours (the pentavalent form) (Gebel 1997, Kentner et al. 1995) Therefore, urinary antimony reflects recent, recent short-term exposure. However, because of the widespread use of antimony in everyday products, assumption of continuous exposure may be reasonable.

CONCLUSION

In this study we found that urinary antimony was associated with higher odds to experience insufficient sleep, increased sleep-onset latency, OSA, sleep problems, and daytime sleepiness. Because of the vast public health implications of sleep disorders, further studies, such as well-designed prospective studies to evaluate the effect of antimony exposure and the risk of developing sleep disorders, are needed to better understand the implications of this study’s findings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Disclaimer: The findings and conclusion in this report are those of the authors and do not necessarily represent the official position of CDC/ATSDR.

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Table 1

Sample size (n) and weighted characteristics of adult participants (20 years of age and older) in NHANES 2005–2008

	n	(%) (SE) Weighted
Urinary Antimony (μg/L), GM (SE)	2654	0.06 (0.002)
Age (Years), GM (SE)	2654	44.21 (0.54)
Urinary Creatinine, GM (SE)	2654	95.93 (1.52)
BMI (kg/m^2), GM (SE)	2654	27.83 (0.21)
Income, GM (SE)	2654	2.55 (0.07)
Serum Cotinine (ng/mL), GM (SE)	2654	0.42 (0.05)
Inactive days due to phys./mental health	2654	5.50 (0.34)
Sex		
Men, % (SE)	1373	49.62 (1.00)
Women, % (SE)	1281	50.38 (1.00)
Race/Ethnicity		
Non-Hispanic White, % (SE)	1374	74.03 (2.35)
Non-Hispanic Black, % (SE)	551	10.31 (1.28)
Hispanic, % (SE)	642	11.41 (1.35)
Other, % (SE)	87	4.25 (0.75)
Smoking Status		
Current Smokers, % (SE)	584	22.69 (1.13)
Former Smokers, % (SE)	727	26.79 (1.38)
Never Smokers, % (SE)	1343	50.52 (1.35)
Alcohol Consumption		
No Alcohol, % (SE)	798	25.13 (1.60)
1–4 drinks per week, % (SE)	1656	66.89 (1.77)
>4 drinks per week, % (SE)	200	7.98 (0.65)
Education Level		
Less than High School, % (SE)	775	18.75 (1.44)
Completed High School, % (SE)	613	24.12 (1.17)
More than High School, % (SE)	1266	57.13 (1.95)
Sleep Duration		
≤ 6 hrs/night, % (SE)	1028	36.67 (1.44)
7–8 hrs/night, % (SE)	1433	56.24 (1.45)
≥ 9 hrs/night, % (SE)	191	7.16 (0.55)
Sleep Onset Latency Time		
≤ 5 min, % (SE)	779	30.30 (1.12)
5–30 min, % (SE)	1354	51.96 (1.47)
> 30 min, % (SE)	511	17.74 (1.15)
Sleep Problems		
Yes, % (SE)	809	31.92 (0.96)
No, % (SE)	1845	68.08 (0.96)

	n	(%) (SE) Weighted
Day Sleepiness		
Yes, % (SE)	480	18.68 (1.11)
No, % (SE)	2172	81.49 (1.11)
Sleep Apnea		
Yes, % (SE)	963	36.41 (1.44)
No, % (SE)	1691	63.59 (1.44)
Diabetes		
Yes, % (SE)	292	7.72 (0.53)
No, % (SE)	2362	92.28 (0.53)
CVD		
Yes, % (SE)	1034	32.63 (1.29)
No, % (SE)	1620	67.37 (1.29)
Work		
Not working, % (SE)	1111	32.91 (1.38)
Regular Daytime Schedule, % (SE)	1287	55.41 (1.32)
Regular Evening or Night Shift, Rotating Shift, or Other, % (SE)	256	11.68 (0.56)

Table 2

Adjusted* multinomial logistic regression (odds ratio and 95% confidence interval) of Insufficient Sleep and Excessive Sleep with quartiles of urinary Antimony in NHANES 2005–2008 participants.

	Model 1 (n=3250)	Model 2 (n=2845)	Model 3 (n=2654)
Insufficient Sleep (≤6 hours/night) vs Normal Sleep duration (7–8 hours/night)			
Antimony Q1	1.00	1.00	1.00
Antimony Q2	1.62 (1.24, 2.12)	1.70 (1.24, 2.33)	1.66 (1.19, 2.31)
Antimony Q3	1.78 (1.34, 2.36)	1.89 (1.36, 2.63)	1.93 (1.33, 2.79)
Antimony Q4	1.63 (1.10, 2.42)	1.71 (1.06, 2.74)	1.73 (1.04, 2.91)
p-trend	<0.01	<0.01	0.01
LN antimony	1.19 (1.03, 1.37)	1.22 (1.02, 1.46)	1.22 (1.01, 1.46)
Excessive Sleep (≥9hours/night) vs Normal Sleep duration (7–8 hours/night)			
Antimony Q1	1.00	1.00	1.00
Antimony Q2	1.44 (0.74, 2.84)	1.37 (0.67, 2.80)	1.36 (0.67, 2.77)
Antimony Q3	1.53 (0.62, 3.78)	1.72 (0.69, 4.26)	1.71 (0.73, 4.00)
Antimony Q4	1.28 (0.48, 3.39)	1.38 (0.52, 3.65)	1.44 (0.57, 3.65)
p-trend	0.38	0.39	.0.55
LN antimony	0.98 (0.70, 1.37)	0.99 (0.74, 1.33)	1.03 (0.75, 1.40)

*Model 1: adjusted for urinary creatinine. Model 2: adjusted for the covariates in model 1 plus age, sex, race/ethnicity, smoking status, alcohol use, education level, income level, BMI, and serum cotinine. Model 3: adjusted for covariates in model 2 plus diabetes, CVD, Physical/ mental health and occupation. Urinary Antimony Quartiles: Q1: ≤ 0.03 μg/L; Q2: 0.04–0.06 μg/L; Q3: 0.07–0.10 μg/L; Q4: > 0.10 μg/L. LN Antimony: Natural log-transformed urinary antimony

Table 3

Adjusted* multinomial logistic regression (odds ratio and 95% confidence interval) for sleep onset latency time for adult participants (20 years of age and older) in NHANES 2005–2008.

	Model 1 (n=3250)	Model 2 (n=2845)	Model 3 (n=2654)
Short sleep-onset latency (≤ 5 minutes/night) vs Normal sleep-onset latency duration (6–30 minutes/night).			
Antimony Q1	1.00	1.00	1.00
Antimony Q2	1.07 (0.74, 1.55)	1.08 (0.72, 1.61)	1.11 (0.75, 1.67)
Antimony Q3	1.28 (0.89, 1.85)	1.42 (0.96, 2.09)	1.36 (0.90, 2.04)
Antimony Q4	1.35 (0.85, 2.15)	1.45 (0.90, 2.33)	1.48 (0.88, 2.38)
p-trend	0.32	0.16	0.32
LN antimony	1.05 (0.90, 1.23)	1.09 (0.91, 1.32)	1.08 (0.89, 1.32)
Prolonged sleep-onset latency (> 30 minutes/night) vs Normal sleep-onset latency duration (6–30 minutes/night).			
Antimony Q1	1.00	1.00	1.00
Antimony Q2	1.18 (0.88, 1.58)	0.99 (0.75, 1.29)	1.02 (0.75, 1.38)
Antimony Q3	1.66 (1.14, 2.43)	1.40 (1.00, 1.98)	1.47 (1.04, 2.09)
Antimony Q4	1.72 (1.20, 2.47)	1.40 (1.03, 1.89)	1.41 (1.01, 1.99)
p-trend	0.03	0.22	0.11
LN antimony	1.21 (1.04, 1.41)	1.12 (0.95, 1.32)	1.15 (0.96, 1.37)

*Model 1: adjusted for urinary creatinine. Model 2: adjusted for the covariates in model 1 plus age, sex, race/ethnicity, smoking status, alcohol use, education level, income level, BMI, and serum cotinine. Model 3: adjusted for covariates in model 2 plus diabetes, CVD, Physical/ mental health and occupation. Urinary Antimony Quartiles: Q1: ≤ 0.03 μg/L; Q2: 0.04–0.06 μg/L; Q3: 0.07–0.10 μg/L; Q4: > 0.10 μg/L. LN Antimony: Natural log-transformed urinary antimony

Table 4

Adjusted* logistic regression for sleep outcomes for adult participants (20 years of age and older) in NHANES 2005–2008

	Model 1 (n=3250)	Model 2 (n=2845)	Model 3 (n=2654)
Antimony Q1	1.00	1.00	1.00
Antimony Q2	1.87 (1.42, 2.46)	1.99 (1.43, 2.77)	2.09 (1.50, 2.92)
Antimony Q3	1.41 (1.07, 1.85)	1.35 (0.99, 1.83)	1.32 (0.97, 1.81)
Antimony Q4	1.54 (1.09, 2.17)	1.58 (1.05, 2.38)	1.57 (1.05, 2.34)
p-trend	<0.01	<0.01	<0.01
LN antimony	1.12 (0.98, 1.27)	1.15 (0.99. 1.33	1.14 (0.98, 1.32)
		Sleep Problems	
Antimony Q1	1.00	1.00	1.00
Antimony Q2	1.51 (1.15, 1.99)	1.36 (1.02, 1.81)	1.29 (0.99, 1.71)
Antimony Q3	1.39 (0.98, 1.97)	1.28 (0.87, 1.87)	1.26 (0.88, 1.79)
Antimony Q4	1.75 (1.23, 2.49)	1.57 (1.08, 2.30)	1.55 (1.08, 2.23)
p-trend	0.01	0.06	0.10
LN antimony	1.13 (0.99, 1.29)	1.09 (0.94, 1.26)	1.08 (0.93, 1.24)
		Daytime Sleepiness	
Antimony Q1	1.00	1.00	1.00
Antimony Q2	1.47 (1.04, 2.08)	1.52 (1.05, 2.21)	1.51 (1.00, 2.26)
Antimony Q3	1.24 (0.86, 1.80)	1.25 (0.80, 1.96)	1.19 (0.75, 1.90)
Antimony Q4	1.79 (1.21, 2.65)	1.87 (1.15, 3.02)	1.73 (1.03, 2.90)
p-trend	0.03	0.04	0.10
LN antimony	1.22 (1.06, 1.40)	1.25 (1.06, 1.48)	1.20 (1.00 1.43)

*Model 1: adjusted for urinary creatinine. Model 2: adjusted for the covariates in model 1 plus age, sex, race/ethnicity, smoking status, alcohol use, education level, income level, BMI, and serum cotinine. Model 3: adjusted for covariates in model 2 plus diabetes, CVD, Physical/ mental health and occupation. Urinary Antimony Quartiles: Q1: ≤ 0.03 μg/L; Q2: 0.04–0.06 μg/L; Q3: 0.07–0.10 μg/L; Q4: > 0.10 μg/L. LN Antimony: Natural log-transformed urinary antimony